REMARKS

This Amendment, filed in reply to the Office Action dated September 9, 2009, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 2-6 and 13 are rejected. Claims 2, 4 and 13 are amended herewith solely to improve clarity and conciseness. Support for the recitation in Claim 2 that the claimed method diagnoses or predicts susceptibility to "open angle glaucoma" can be found throughout the specification as originally filed, and at, for example, page 1, lines 10-23. Claims 3, 5 and 6 are canceled herewith without prejudice or disclaimer.

Claims 40-42 are newly added. Support for the subject matter of Claims 40-42 can be found throughout the specification as originally filed, and at, for example, page 1, lines 10-23.

No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Drawings

Applicant thanks the Examiner for acknowledging acceptance of the drawings submitted September 15, 2006.

Information Disclosure Statements

Applicant thanks the Examiner for returning initialed copies of the PTO Forms SB/08 that accompanied the Information Disclosure Statements filed September 15, 2006, and August 13, 2008, indicating consideration of the references therein.

Claims 2, 4 and 13 are Definite Under 35 U.S.C. § 112, second paragraph

On page 3 of the Office Action, Claims 2-6 and 13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

1. In one aspect of the rejection, the Examiner contends that recitation of the phrase "genotype with respect to" renders the claims indefinite, alleging that it is unclear from this recitation whether the claim actually requires that the specifically recited genes be genotyped.

Applicant respectfully points out that the claims as amended do not recite "genotype with respect to," and thus, this aspect of the rejection is moot. Further, Applicant respectfully submits that the claims as amended are definite under section 112, second paragraph.

2. In a second aspect of the rejection, the Examiner contends that the claim language is indefinite inasmuch as it is unclear whether only one polymorphism needs to be detected to confirm diagnosis, or whether all three need to be detected.

Initially, Applicant respectfully submits that, in view of the guidance set forth in the specification as filed, those of ordinary skill in the art would readily be unable to discern the bounds of the claim language; specifically, in light of the working examples in the specification, Applicant respectfully submits that those of ordinary skill in the art would appreciate that the presence of any one of these polymorphisms is sufficient to make a diagnosis, or to make a prediction of susceptibility. Nevertheless, in the interest of compacting prosecution of the Application, and without acquiescing to the merits of the rejection, Applicant herewith amends Claim 2 to recite that "when said subject has at least one polymorphism selected from the group consisting of an adenine at position 462 of the Noelin 2 gene, a cytosine at position 1105 of the Myocilin gene, and an adenine at position 412 of the Optineurin gene, said subject has, or is

susceptible to, open angle glaucoma." Applicant submits that the amendments overcome the rejection.

Withdrawal of the rejection is respectfully requested.

Claims 2, 4 and 13 are Enabled Under 35 U.S.C. § 112, first paragraph

On page 5 of the Office Action, Claims 2-6 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

In making the rejection, the Examiner acknowledges that the specification is enabling for a method for diagnosing, or predicting susceptibility to, *primary open angle glaucoma* in a human, comprising testing a biological sample from a human to identify the nucleotides present at position 462 of the noelin 2 gene, position 1105 of the myocilin gene, and position 412 of the optineurin gene, and determining that the subject has, or is susceptible to having, primary open angle glaucoma when the subject has any of the following: an adenine at position 462 of the noelin 2 gene, a cytosine at position 1105 of the myocilin gene, or an adenine at position 412 of the optineurin gene. Moreover, the Examiner takes the position that normal-tension glaucoma is a subset of primary open angle glaucoma, and accordingly, is also enabled subject matter.

However, the Examiner contends that the specification is not enabling for a method of diagnosing, or predicting susceptibility to, any type of optic neuropathy, any type of glaucoma, or Leber's disease. The Examiner further contends that it would be highly unpredictable as to which other types of glaucomas and optic neuropathies could be diagnosed, or the susceptibility thereto predicted, by detecting any of the claimed polymorphisms. On this basis, the Examiner alleges that one of skill in the art would have to embark on undue experimentation to practice the full scope of the claims.

Initially, Applicant notes that Claims 3, 5 and 6 are canceled herewith without prejudice or disclaimer, mooting the rejection of these claims.

Further, solely in the interest of compacting prosecution, and without acquiescing to the merits of the rejection, Applicant herewith amends Claim 2 to recite a method for diagnosing or predicting susceptibility to "open angle glaucoma," commensurate in scope with the subject matter the Office indicates as being enabled by the specification; specifically, while the Examiner contends that normal-tension glaucoma is a *subset* of primary open angle glaucoma, and thus is encompassed *and* enabled by a method for diagnosing or predicting susceptibility to primary open angle glaucoma, Applicant respectfully points out that normal-tension glaucoma and primary open angle glaucoma are more properly considered to both be subsets of *open angle glaucoma*. For example, as noted on page 1 of the specification as filed, one significant difference between normal-tension glaucoma and primary open angle glaucoma is the extent of the increase in intraocular pressure. Further, that normal-tension glaucoma and primary open angle glaucoma are more properly considered subsets of *open angle glaucoma* is corroborated by technical literature. For example, consistent with the description in the specification as filed, Table 7.2 of the attached literature reference R. Rand Allington *et al.*, Shields' Textbook of Glaucoma, 5th ed., Lippincott Williams & Wilkins (2005), pp. 156-7, evidences that primary (chronic) open angle glaucoma and normal-tension glaucoma were recognized in the art at the time of the invention as being different subsets of *open-angle glaucoma* (the right column on page 156 indicates that primary open-angle glaucoma is another name for chronic open-angle glaucoma)..

As evidenced by the working examples in the specification as filed, and as acknowledged by the Office, the specification is enabling for a method for diagnosing, or predicting

susceptibility to, primary open angle glaucoma and normal-tension glaucoma in a human, comprising testing a biological sample from a human to identify the nucleotides present at position 462 of the noelin 2 gene, position 1105 of the myocilin gene, and position 412 of the optineurin gene, and determining that the subject has, or is susceptible to having, open angle glaucoma when the subject has any of the following: an adenine at position 462 of the noelin 2 gene, a cytosine at position 1105 of the myocilin gene, or an adenine at position 412 of the optineurin gene. Because primary open angle glaucoma and normal-tension glaucoma are thus both subsets of open angle glaucoma, Applicant respectfully submits that the specification is similarly enabling for the presently claimed subject matter.

Withdrawal of the rejection is respectfully requested.

Claims 2, 4 and 13 are Patentable Under 35 U.S.C. § 103

On page 12 of the Office Action, Claims 2-6 and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ishikawa *et al.* (*J. Glaucoma*, 2004, 13(6):466-471) in view of Umeda *et al.* (*Invest Ophthalmol Vis. Sci.*, 2003, 44: E-Abstract 1111) and Mukhopadhyay *et al.* (*Molecular Vision*, 2004, 10:304-314).

In making the rejection, the Examiner contends that Ishikawa *et al.* discloses identification of the 1105 T>C polymorphism in the myocilin gene in a patient with primary open angle glaucoma, and allegedly discloses diagnosing or predicting susceptibility to optic neuropathy based on genotyping for this polymorphism. However, the Examiner acknowledges that Ishikawa *et al.* does not disclose genotyping for the 412G>A polymorphism in the optineurin gene. In an attempt to rectify such deficiency, the Examiner cites to Umeda *et al.*, who allegedly discloses determining the genotype of a glaucoma patient sample for the 412G>A

polymorphism of the optineurin gene. However, the Examiner acknowledges that neither Ishikawa *et al.* nor Umeda *et al.* discloses genotyping a sample to detect a CGG to CAG substitution at codon 144 of the noelin 2 gene.

The Examiner contends that such deficiency is rectified by Mukhopadhyay *et al.*, who allegedly discloses noelin-2 as a candidate gene associated with eye disorders, such as primary open angle glaucoma, because it is expressed in the eye and shares olfactomedin domains with myocilin, citing the Abstract.

The Examiner takes the position that, in view of Umeda *et al.* and Mukhopadhyay *et al.*, one of ordinary skill in the art would readily have modified the method of Ishikawa *et al.* to further genotype for the 412G>A polymorphism in the optineurin gene and the CGG to CAG substitution at codon 144 of the noelin 2 gene. The Examiner contends that one of ordinary skill in the art would have possessed sufficient motivation to make such a combination, in order to identify genetic mutations associated with eye disorders, and "because early detection results in early treatment which can postpone or prevent loss of vision."

Applicant respectfully disagrees, and traverses the rejection in view of the following remarks.

Initially, Applicant respectfully points out that the Ishikawa *et al.* article was published in December 2004, less than one year prior to the filing date of the International Stage Application, namely March 18, 2005, and therefore only qualifies as legally effective prior art to support the outstanding obviousness rejection under section 102(a)/103. Moreover, Applicant respectfully points out that Ishikawa *et al.* describes Applicant's own work and inventive effort. Accordingly, Applicant submits herewith a Rule 132 Declaration establishing that the authors of Ishikawa *et al.* derived their knowledge from Applicant, such that Ishikawa *et al.* does not

qualify as legally effective prior art to the instant Application. Because neither Umeda *et al.* nor Mukhopadhyay *et al.* discloses or suggests identification of the 1105 T>C polymorphism in the myocilin gene, much less in a patient with primary open angle glaucoma, even assuming *arguendo* that one of ordinary skill in the art were to combine Umeda *et al.* and Mukhopadhyay *et al.* in the manner asserted in the rejection, they would not arrive at the presently claimed invention. Accordingly, the cited references, taken alone or in combination, do not render obvious the presently claimed method.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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